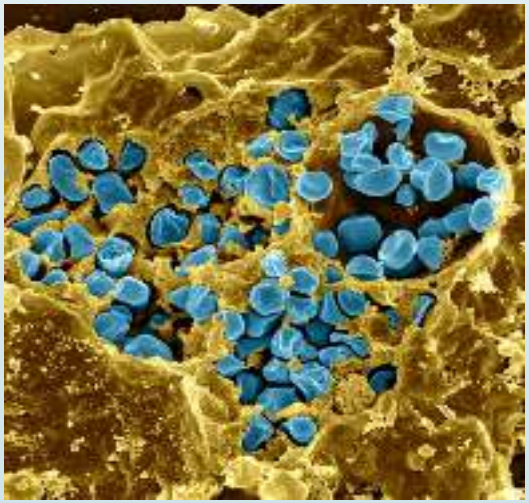
Tularemi

Dr. Esra KAYA KILIÇ
Ankara Eğitim ve Araştırma Hastanesi
EKMUD Ankara Günleri
08/11/2017



Olgu

- 60 yaş
- Kadın hasta
- Ateş
- Üşüme-titreme
- Halsizlik
- Bulantı-kusma

Bir haftadır

- Sefuroksim aksetil 2x500 mg tb

Fizik muayene;

- Ateş 38,4 C
- TA: 120/80 mmHg
- Posterior servikal bölgede ülseratif nodüler lezyonla birlikte 3×1 cm ve 1×1 cm boyutlarında bölgesel lenfadenopati
- Hepatomegali (kot altı 1 cm)
- 1 hafta önce kene teması +

Laboratuvar;

- Lökosit: 7100/mm^3
- Trombosit: 156 000/mm^3
- Hb: 13.7 gr/dl
- ESR: 21 mm/saat
- CRP: 2.5 mg/lt
- Karaciğer ve böbrek fonksiyon testleri, serum elektrolitleri, kreatin kinaz ve kanama profili normal sınırlarda

- Anteroposterior servikal bölgenin ultrasonografisinde;

- Solda en büyüğü 24×100 mm boyutlarında olmak üzere difüz kortikal kalınlaşma gösteren birkaç reaktif lenf gangliyonu

- Doksisiklin 2x100 mg tb
- Yatışının üçüncü gününde yaygın halsizlik ve boyun ağrısı yakınmaları geriledi Doksisiklin tedavisiyle CRP ve ESH değerleri normale döndü.
- MAT 1/20 (temasın birinci haftasında)
- MAT 1/160 (temasın ikinci haftasında)
- 14 gün oral tedavi

- Francis hastalığı
- Geyik sineği ateşi
- Tavşan ateşi
- Su-fare avcısı hastalığı
- Yabani tavşan hastalığı
- Ohara hastalığı

FRANCIS EDWARD STEWART, PH.G., M.D., PHAR.D.

- Tularemi *Francisella tularensis* kaynaklı bir zoonoz.
- *F. tularensis*
  - hareketsiz,
  - pleomorfik,
  - gram negatif bir kokobasil
- Soğuk ve nemli ortamlara haftalarca canlı kalacak şekilde dayanıklı
- Güneş ışığı, yüksek ısı ve klora dayanıksız.

Özellik	*F. Tularensis* Subtipleri			*F. philomiragia*	*F. hispaniensis*
	tularensis (Tip A)	*holarctica (Tip B)*	*novicida*		
Sistein gereksimi	+	+	-	-	-
%6 NaCl ilaveli buyyonda büyüme	-	-	+	+	Elde veri yok
Hareket	-	-	-	-	Elde veri yok
Oksidaz	-	-	-	+	+
Nitrat indirgeme	-	-	-	-	Elde veri yok
Asit form					
Glukoz	+	+	+	+	+
Gliserol	+	-	+	+	Elde veri yok
Jelatin hidrolizi	-	-	-	Değişken	Elde veri yok
Virülans					
İnsan	Yüksek	Orta	Düşük	Düşük	Düşük
tavşan	Yüksek	Düşük	Düşük	Elde veri yok	Elde veri yok

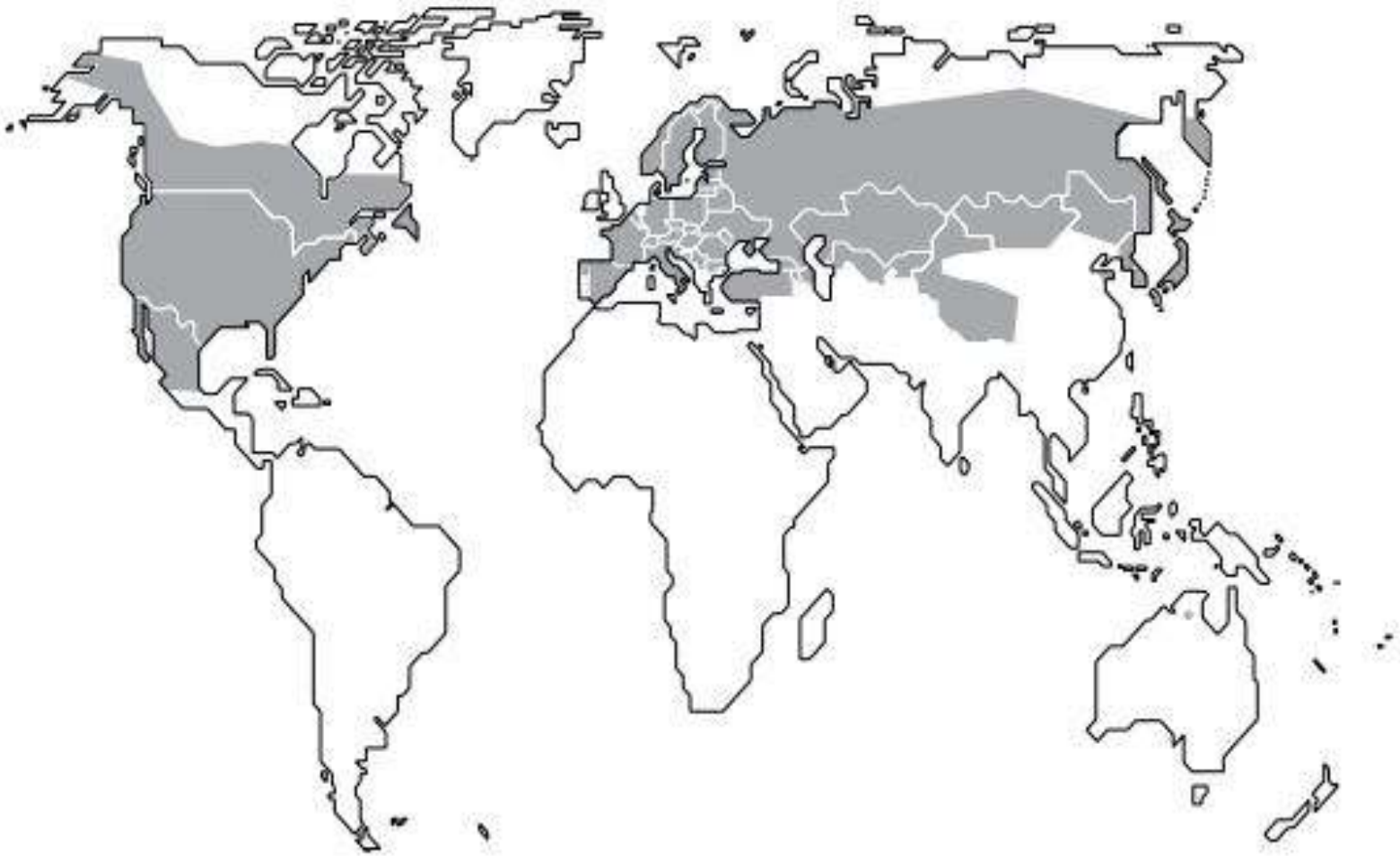


Figure 3.1 The geographical distribution of tularaemia is indicated in grey. Locally, the disease often has an uneven distribution with recurrent epidemic outbreaks in geographically restricted areas. The data were compiled from publications in the medical literature between 1952–2006. Credit: Anders Johansson, Umeå University, Umeå, Sweden and from a recent publication (de Carvalho et al., 2007)

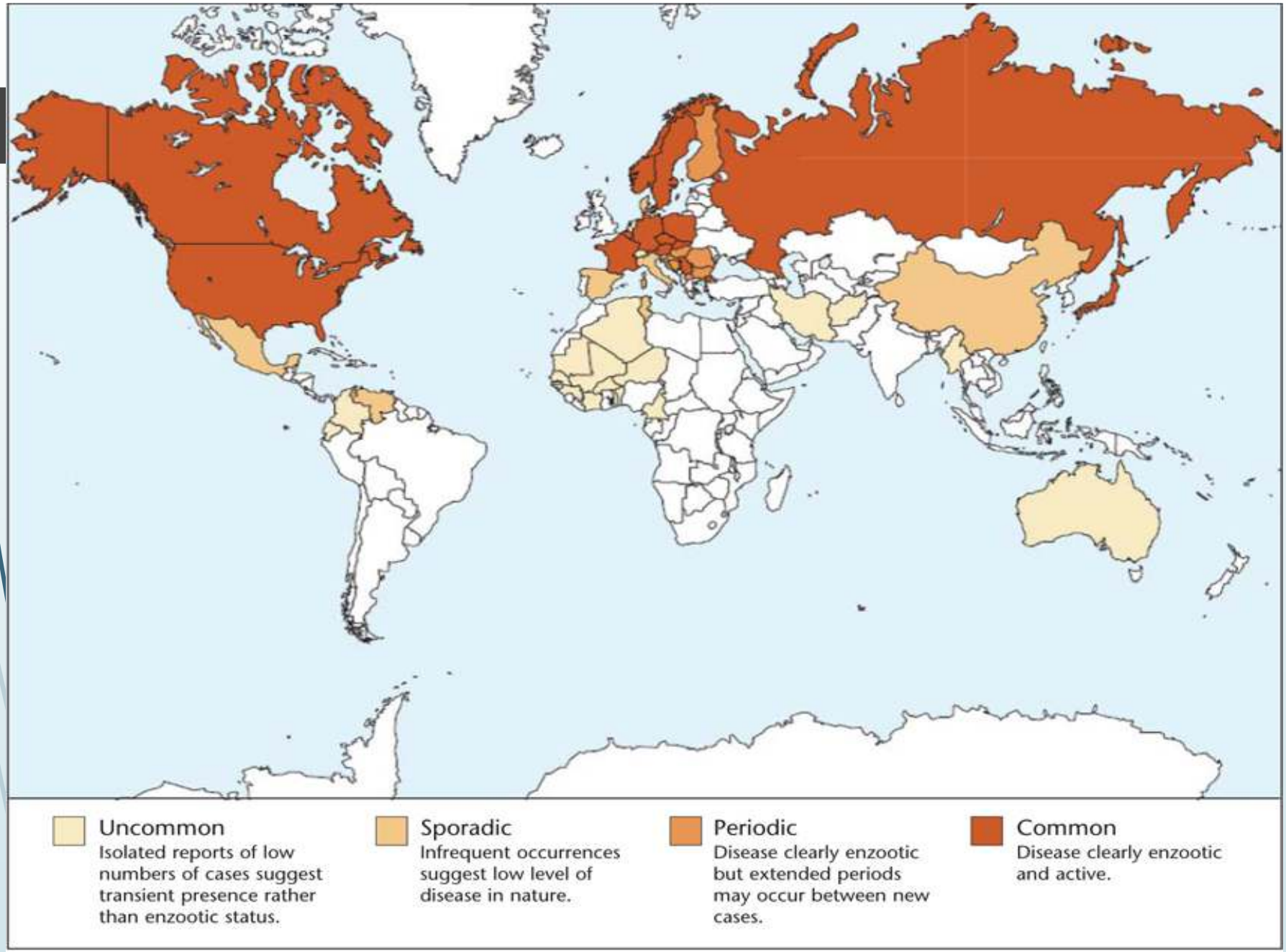
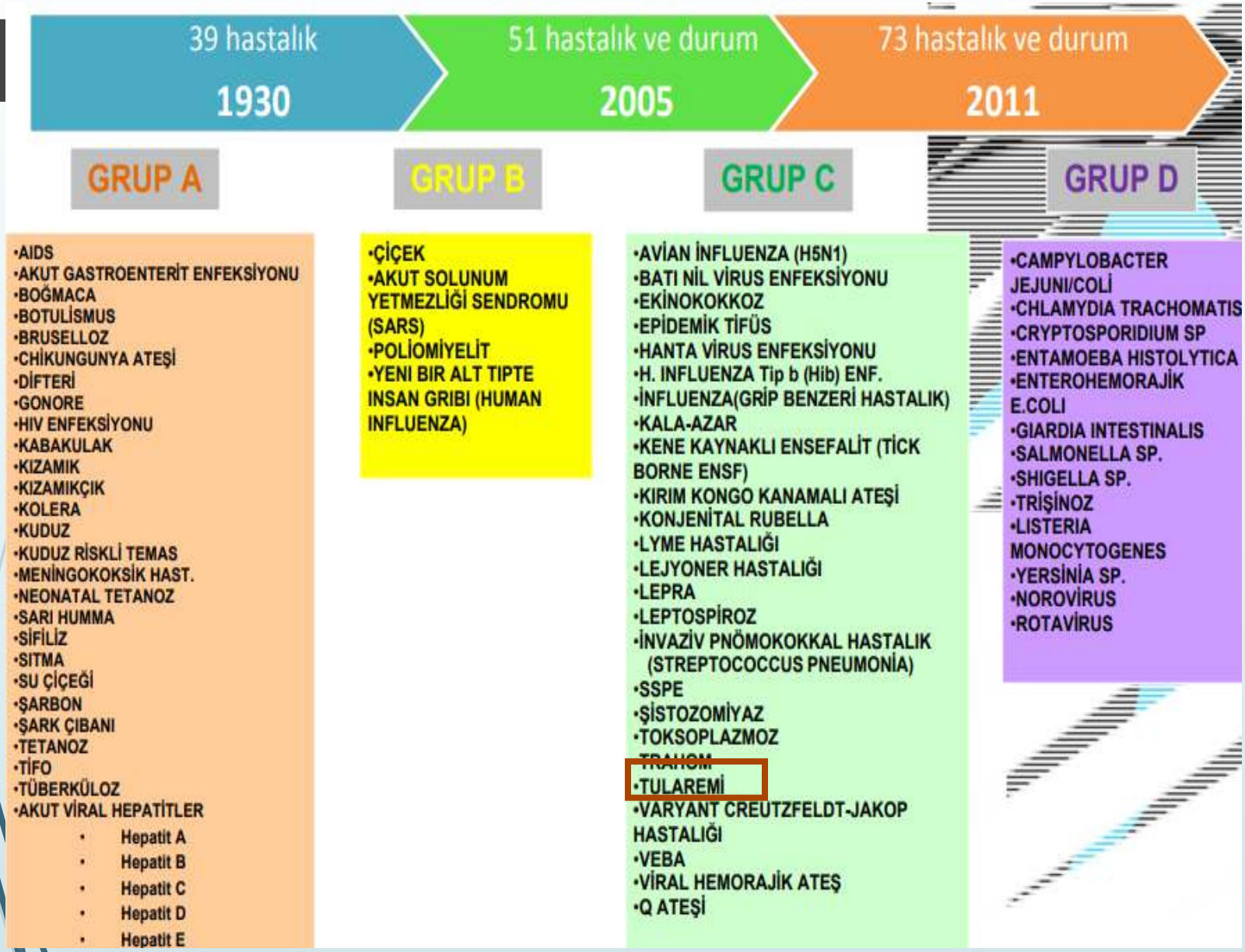


Figure 3. Worldwide occurrence of tularemia.

- Tip A suşlar genellikle Kuzey Amerika' da
  - Slovakya
  - Avusturya
- Tip B suşlar kuzey yarımkürede
  - Tazmanya
- Avrupa' da genellikle tip B suşlar ile Tularemi görülmekte

- *F. tularensis holarctica*
  - Biovar 1 (eritrosin duyarlı)
    - Batı Avrupa
  - Biovar 2 (eritrosin dirençli)
    - Doğu Avrupa
  - Biovar japonica (gliserolü fermente eder)
    - Japonya, Çin,Türkiye



2001'de CDC tarafından Kategori A potansiyel biyoterorizm ajanı olarak tanımlanmış

- 2001’ de CDC tarafından Kategori A potansiyel biyoterorizm ajanı olarak tanımlanmış
- 2005 yılında itibaren ülkemizde C grubu bildirimi zorunlu hastalıklar listesinde

Bulaş

- İnsandan insana geçiş saptanmamış
- İnsanlara bulaşma:
  - Artropod ve ısırıkları
  - İnfekte hayvan, infeksiyöz hayvana ait doku ya da sıvılar
  - Kontamine su veya yiyecek yenilmesi
  - İnfektif aerosollerin inhalasyonu

Bulaş

- *F.tularensis tularensis*
  - Bulaşmada tavşan, koyun ve kene
- *F.tularensis holarctica*
  - Bulaşmada misk sıçanı, kunduz gibi suyla yaşamsal ilişkisi olan çok sayıda vektör

ISABELLE PELLOUX[4], MAX MAURIN[4], JOCELYNE CAILLON[1], PHILIPPE MOREAU[5], JEAN-FRANÇOIS YGOUT[3] & STÉPHANE CORVEC[1]

From the [1]Service de Bactériologie-Hygiène, CHU de Nantes, Nantes, [2]Unité de Bactériologie, CHRU de Brest, Brest, EA 3882-LUBEM, SFR148 ScInBioS, Université de Brest, Brest, [3]Laboratoire de Biologie, CH de Bretagne Sud, Lorient, [4]Centre National de Référence des Francisella, CHU de Grenoble, Grenoble, and [5]Service d'Hématologie, CH de Bretagne Sud, Lorient, France

Fransa' da **donma** tehlikesi yaşayan bir hasta

Akarsuda donma tehlikesinden 5 gün sonra yüksek ateş

Kan kx *F. tularensis*

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Dec. 2009, p. 7488–7500 Vol. 75, No. 23
0099-2240/09/$12.00 doi:10.1128/AEM.01829-09

Francisella tularensis Type A Strains Cause the Rapid Encystment of *Acanthamoeba castellanii* and Survive in Amoebal Cysts for Three Weeks Postinfection[▽]

Sahar H. El-Etr,[1]* Jeffrey J. Margolis,[2] Denise Monack,[2] Richard A. Robison,[3] Marissa Cohen,[3] Emily Moore,[3] and Amy Rasley[1]

Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory, Livermore, California 94550[1]; Department of Microbiology and Immunology, Stanford University Medical School, Stanford, California 94305[2]; and Department of Microbiology and Molecular Biology, Brigham Young University, Provo, Utah 84602[3]

Received 29 July 2009/Accepted 29 September 2009

***Francisella tularensis*, the causative agent of the zoonotic disease tularemia, has recently gained increased attention due to the emergence of tularemia in geographical areas where the disease has been previously unknown and to the organism's potential as a bioterrorism agent. Although *F. tularensis* has an extremely broad host range, the bacterial reservoir in nature has not been conclusively identified. In this study, the ability of virulent *F. tularensis* strains to survive and replicate in the amoeba *Acanthamoeba castellanii* was explored. We observe that *A. castellanii* trophozoites rapidly encyst in response to *F. tularensis* infection and that this rapid encystment phenotype is caused by factor(s) secreted by amoebae and/or *F. tularensis* into the coculture medium. Further, our results indicate that in contrast to the live vaccine strain LVS, virulent strains of *F. tularensis* can survive in *A. castellanii* cysts for at least 3 weeks postinfection and that the induction of rapid amoeba encystment is essential for survival. In addition, our data indicate that pathogenic *F. tularensis* strains block lysosomal fusion in *A. castellanii*. Taken together, these data suggest that interactions between *F. tularensis* strains and amoebae may play a role in the environmental persistence of *F. tularensis*.**

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- Kedi, köpek veya diğer hayvanlara sahip olanlar,
- Golf sahaları ve ormanları ziyaret edenler,
- Farklı türde tarım işleriyle uğraşanlar,
- Ölü hayvanlarla eldiven olmadan temas edenler,
- Göl veya nehirlerde yüzenler,
- Göl veya kuyulardan su içenler,
- Sivrisinek, kene, geyik sinekleri ya da diğer böcekler tarafından ısırılanlar
- Laboratuvar çalışanları, veteriner hekimler

TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
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doi:10.3906/sag-1412-138

The prevalence of tularemia in occupational groups that have contact with animals

Fatih BÜYÜK[1,*], Özgür ÇELEBİ[1], Elif ÇELİK[1], Bekir ÇELEBİ[2], Selçuk KILIÇ[2], Aliye GÜLMEZ SAĞLAM[1], Doğan AKÇA[3], Mehmet DOĞANAY[4], Salih OTLU[1], Mitat ŞAHİN[1]

[1]Department of Microbiology, Veterinary Faculty, University of Kafkas, Kars, Turkey
[2]Public Health Institution of Turkey, National Tularemia Reference Laboratory, Ankara, Turkey
[3]Kars Health School, University of Kafkas, Kars, Turkey
[4]Department of Infectious Diseases, Faculty of Medicine, University of Erciyes, Kayseri, Turkey

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210 kan örneği incelenmiş
- 103 çiftçi, 45 veteriner, 42 kasap, 11 gönüllü

MA ve ELISA ile %7,46 (+)
- Çifçiler %13,5
- Veterinerler %2,2

disease in the northeast of Turkey.

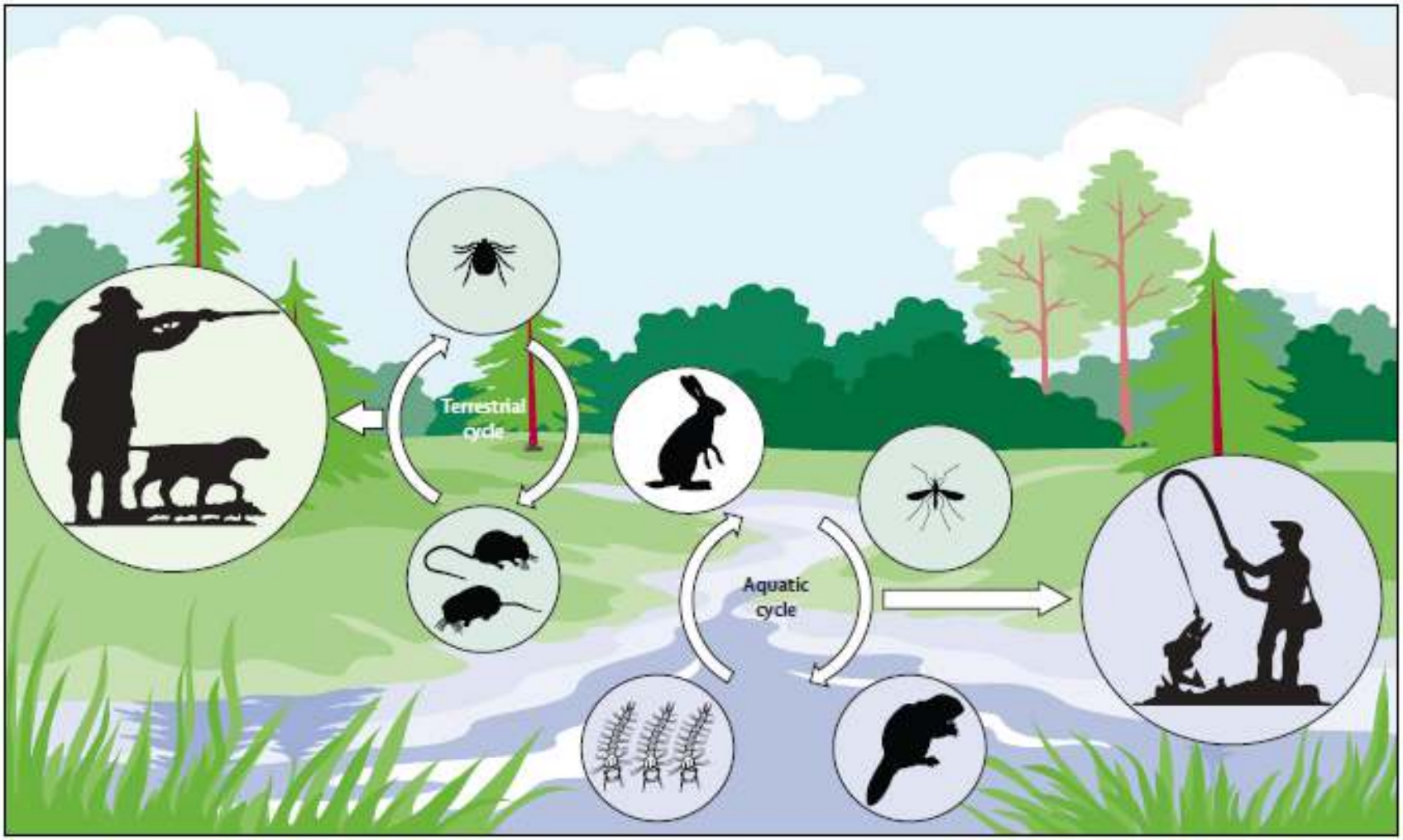


Figure 1: **The two main lifecycles—terrestrial and aquatic—of *Francisella tularensis* in Europe**
Ticks and rodents are reservoir hosts in the terrestrial cycle. Lagomorphs, mosquitoes, mosquito larvae, and rodents are reservoirs in the aquatic cycle.

Lancet Infect Dis 2016;16: 113–24

Tularemia Epidemic in Northwestern Spain: Clinical Description and Therapeutic Response

José Luis Pérez-Castrillón, Pablo Bachiller-Luque, Miguel Martín-Luquero, Francisco Javier Mena-Martín, and Vicente Herreros

Department of Internal Medicine, Rio Hortega Hospital, University of Valladolid, Valladolid, Spain

This study describes the clinical characteristics of tularemia in Spain's first epidemic outbreak and the therapeutic response and compares the efficacy of 3 antibiotics (streptomycin, ciprofloxacin, and doxycycline). For 142 cases of tularemia, the therapeutic failure rate was 22.5%; ciprofloxacin was the antibiotic with the lowest percentage of therapeutic failures and with the fewest side effects.

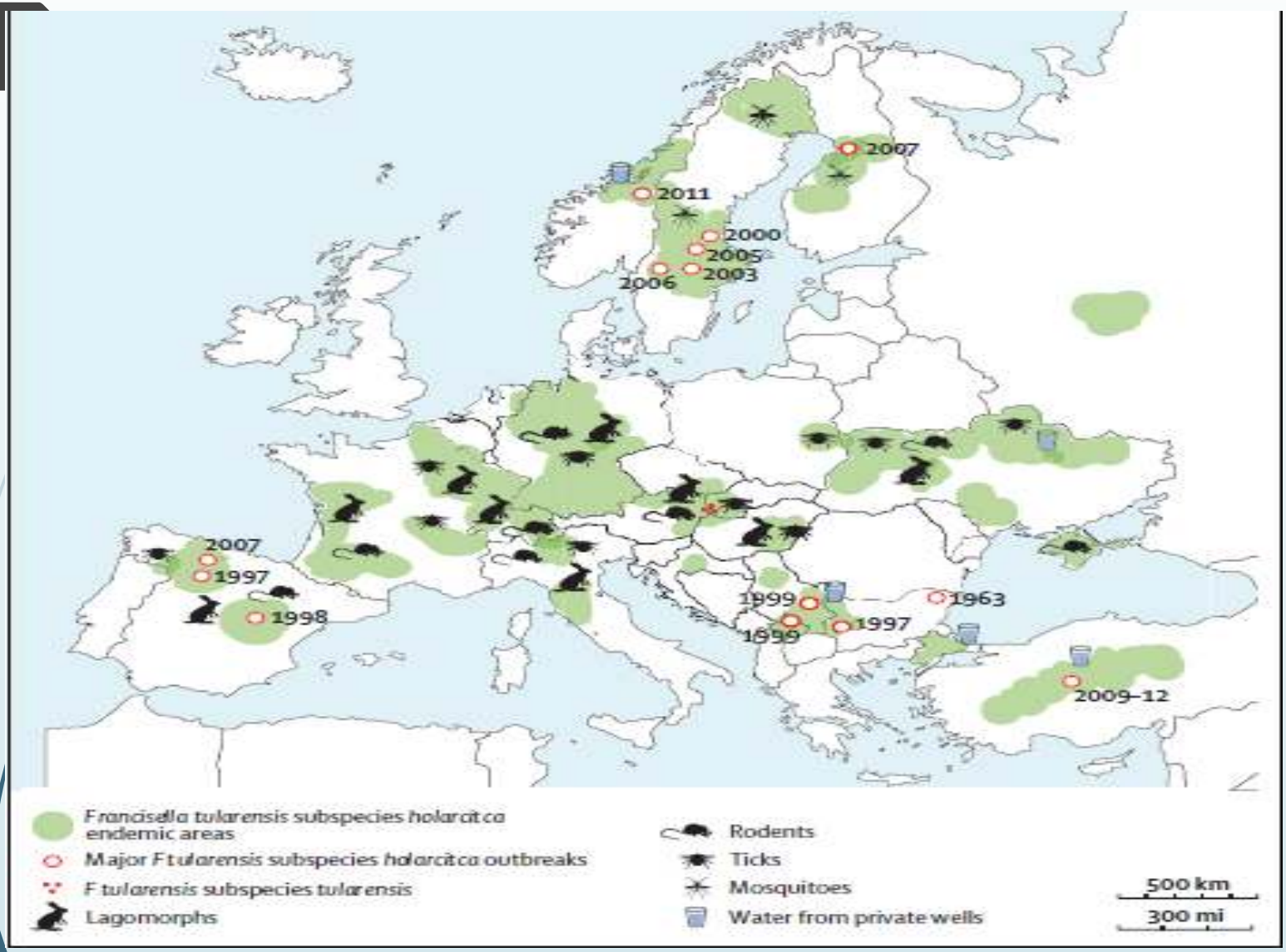
Waterborne Outbreak of Tularemia Associated with Crayfish Fishing

Pedro Anda,* Javier Segura del Pozo,*† José María Díaz García,‡ Raquel Escudero,* F. Javier García Peña,§ M. Carmen López Velasco,‡ Ricela E. Sellek,* M. Rosario Jiménez Chillarón,‡ Luisa P. Sánchez Serrano,* and J. Fernando Martínez Navarro*

*Instituto de Salud Carlos III, Majadahonda, Madrid, Spain; †Public Health Department, Alcalá de Henares, Madrid, Spain; ‡Cuenca Public Health Department, Cuenca, Spain; and §Ministry of Agriculture and Fisheries, Algete, Madrid, Spain

In 1997, an outbreak of human tularemia associated with hare-hunting in central Spain affected 585 patients. We describe the identification of *Francisella tularensis* biovar palaearctica in a second outbreak of ulceroglandular tularemia associated with crayfish (*Procambarus clarkii*) fishing in a contaminated freshwater stream distant from the hare-associated outbreak. The second outbreak occurred 1 year after the first.

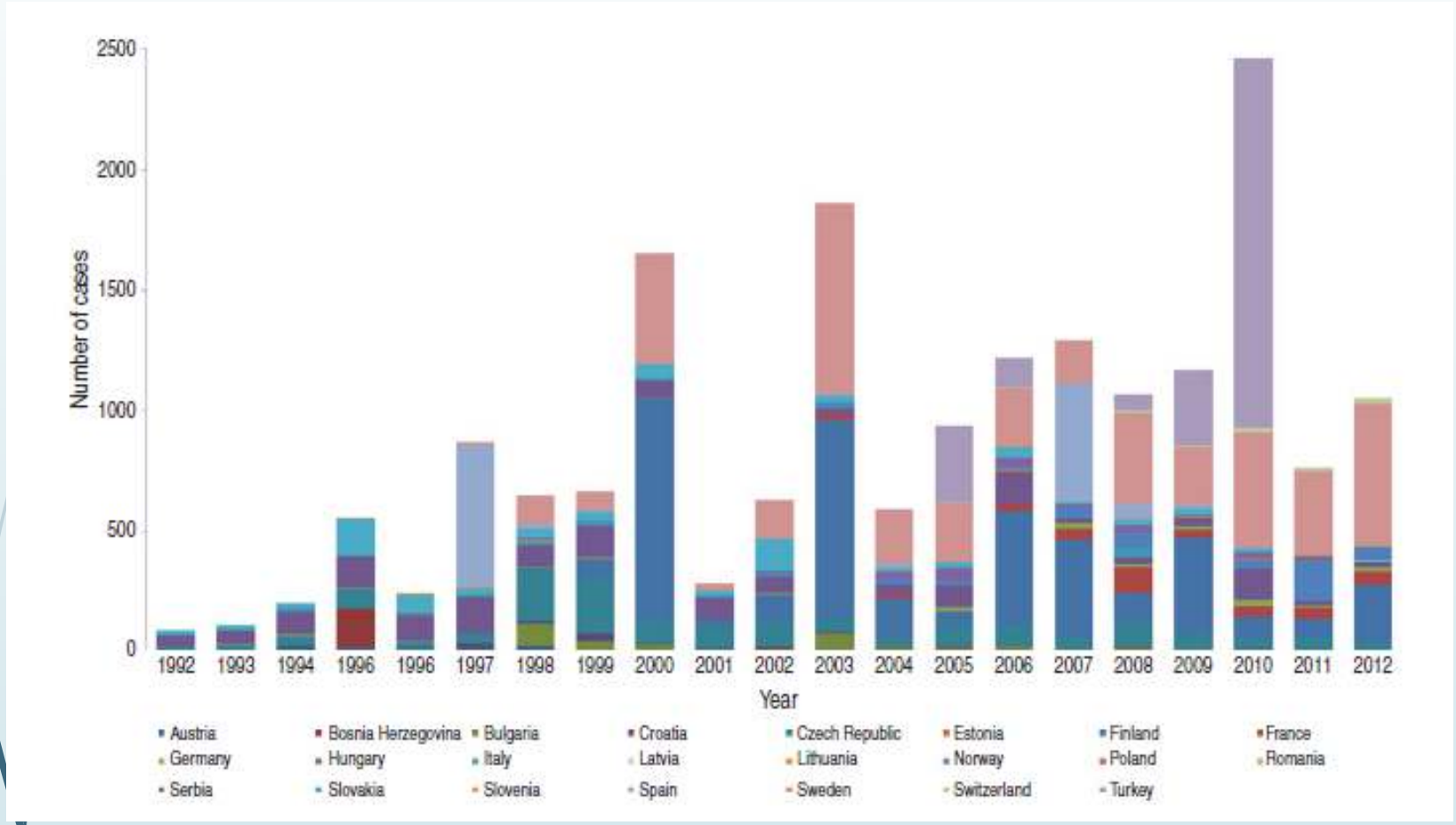
İspanya' da hem karasal hem de su kaynaklı bir salgın
142 ve 595 vaka



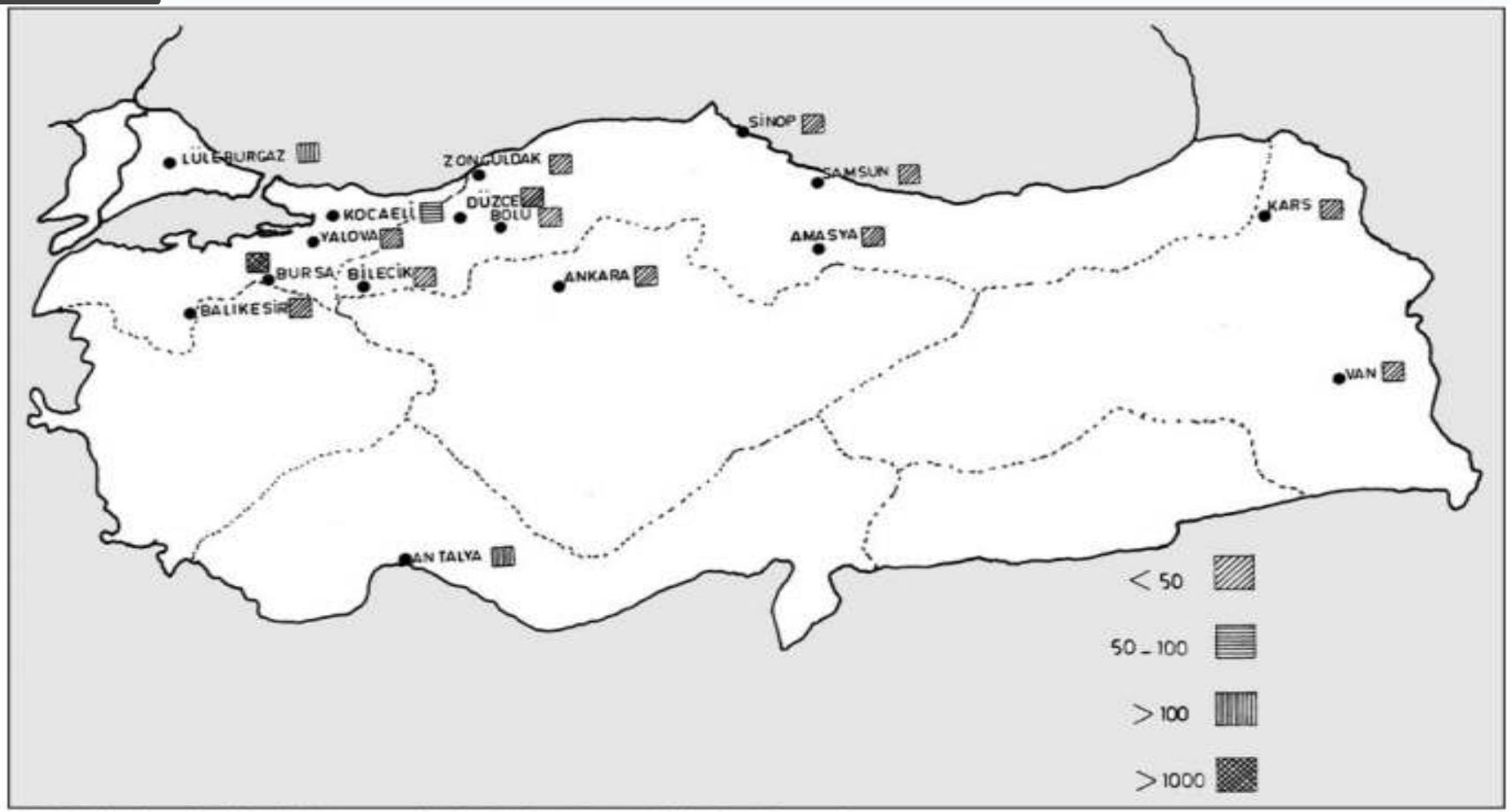
Lancet Infect Dis 2016;16: 113–24

	Most predominant environment for lifecycle	Most predominant modes of transmission	Most predominant modes of clinical forms	Known endemic areas
Austria[53,85]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Lower Austria, Burgenland, Vienna, Styria, and Upper Austria
Bulgaria[43]	Aquatic	Consumption of contaminated water	Oropharyngeal	Sofia and Pernik provinces
Czech Republic[58]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Moravia
Finland[59]	Aquatic	Mosquito bites	Ulceroglandular and glandular, oropharyngeal	Oulu
France[50]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Eastern, central, and southwestern parts of the country
Germany[54,86]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Bavaria, Hesse, Baden-Wuerttemberg, Thuringia, and Lower Saxony
Hungary[55]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Csongrád, Békés, Hajdú-Bihar, Győr-Moson-Sopron, Heves, and Jász-Nagykun-Szolnok
Italy[47]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Lombardy, and Tuscany
Kosovo[42]	Aquatic	Consumption of contaminated water	Oropharyngeal	Rural areas in the whole country
Norway[22,43,88]	Aquatic	Consumption of contaminated water	Oropharyngeal	Central and northern parts of the country
Serbia[89]	Aquatic	Consumption of contaminated water	Oropharyngeal	Nišava, Zajecar, Pirot, Pčinja, Toplica, Rasina, and Belgrade districts
Slovakia[64]	Terrestrial	Direct contact with animal reservoirs, through tick bites	Ulceroglandular and glandular	Western part of the country
Spain[44,66,90]	Terrestrial and aquatic	Direct contact with animal reservoirs, through tick bites, catching crayfish	Ulceroglandular and glandular, typhoidal	Valladolid, Palencia, Leon, and Cuenca provinces
Sweden[20,83]	Aquatic	Mosquito bites	Ulceroglandular and glandular	Northern and central parts of the country
Turkey[91]	Aquatic	Consumption of contaminated water	Oropharyngeal	Central Anatolia

Lancet Infect Dis 2016;16: 113–24



G. Hestvik and others. Epidemiol. Infect., Page 1 of 24.
2014 doi:10.1017/S0950268814002398



Şekil-1. Türkiye'de serolojik olarak tularemi tanısı konulan olguların illere göre dağılımı (□:Olgu sayısı)

Akalın H. Ülkemizde Tularemi sorunu, 7. İç Hastalıkları Ulusal Kongresi 2005

Figure 5. Provinces in which tularemia has been recorded according to tularemia epidemics or serologically confirmed cases.

KILIÇ S Francisella tularensis ve Türkiye'de Tularemi Epidemiyolojisine Genel Bir Bakış, Flora, 2010;15(2):37-58

Tablo 1. 1936-2005 yılları arasında ülkemizde bildirilen tularemi salgınları

Yıl	Bölge	Vaka	Mevsim	Bulaşma
1936	Lüleburgaz	150	Yaz	Su kaynaklı
1937	Tatvan	6		Gıda
1945	Lüleburgaz	18	İlkbahar	Su kaynaklı
1953	Antalya	200	Sonbahar	Su kaynaklı
1988 - 2002	Bursa	205	Kış	Su kaynaklı
1997	Ankara	16	Kış	Su kaynaklı
2000	Düzce	21	Sonbahar	Su kaynaklı
2001	Bolu	14	Sonbahar	Su kaynaklı
2002	Balıkesir	115	Kış	Su kaynaklı
2004	Suluova	43	Sonbahar	Su kaynaklı
2004 - 2005	Zonguldak	61	Kış	Su kaynaklı
2004 - 2005	Kocaeli	145	Kış-ilkbahar	Su kaynaklı
2004 - 2005	Kars	56	Kış-ilkbahar Sonbahar	Su kaynaklı
2005	Kocaeli	129	Kış	Su kaynaklı
2005	Tokat	8	Kış	Su kaynaklı
2005	Edirne	10	Kış	Su kaynaklı
2005	Düzce	11	Kış	Su kaynaklı

TULAREMİ - Vaka ve Ölüm Sayıları, Morbidite ve Mortalite Hızları, Türkiye, 2006-2016

Yıllar	Nufus	Vaka Sayısı	Morbidite Hızı (100.000)	Ölüm Sayısı	Mortalite Hızı (1.000.000)
2006	72.974.000	126	0,17	0	0,00
2007	70.586.256	89	0,13	0	0,00
2008	71.517.100	71	0,10	0	0,00
2009	72.561.312	428	0,59	0	0,00
2010	73.722.988	1531	2,08	0	0,00
2011	74.724.269	2151	2,88	0	0,00
2012	75.627.384	607	0,80	0	0,00
2013	76.667.846	218	0,28	0	0,00
2014	77.695.904	132	0,17	0	0,00
2015	78.741.053	347	0,44	0	0,00
2016	79.814.871	491	0,62	0	0,00

Özgün Çalışma/Original Article

Mikrobiyol Bul 2011; 45(1): 58-66

Orta Anadolu Bölgesi İllerinden Hastanemize Başvuran Orofaringeal Tularemi Olgularının Değerlendirilmesi

Ocak-Mayıs aylarında
Çorum, Ankara, Kırşehir,Yozgat
10 hasta

Evaluation of th Cases Admitted to Our Hospital from the Provinces of Central Anatolia

Melek UYAR[1], Buğra CENGİZ[1], Murat ÜNLÜ[1], Bekir ÇELEBİ[2], Selçuk KILIÇ[2], Adil ERYILMAZ[1]

[1] SB Ankara Numune Eğitim ve Araştırma Hastanesi, 3. Kulak Burun Boğaz Kliniği, Ankara.
[1] *Ankara Numune Education and Research Hospital, 3rd Ear, Nose & Throat Department, Ankara, Turkey.*

[2] Refik Saydam Hıfzıssıhha Merkezi, Ulusal Tularemi Referans Laboratuvarı, Ankara.
[2] *Refik Saydam Hygiene Center Presidency, National Reference Laboratory for Tularemia, Ankara, Turkey.*

Editöre Mektup/Letter to Editor Mikrobiyol Bul 2011; 45(4): 762-764

Orta Anadolu Kaynaklı Tularemi Olgularının Değerlendirilmesi

Evaluation of Tularemia Cases Originated from Central Anatolia, Turkey

Aralık 2009-Kasım 2010 arasında

Ankara, Kırşehir, Çankırı, Çorum, Yozgat, Hakkari illerinden

32 hasta

Avcılık ve av eti yeme gibi riskli davranışlar hiç bir hastada tespit edilmemiştir

Hastaların hepsinde boyunda şişlik

Özgün Çalışma/Original Article Mikrobiyol Bul 2012; 46(2): 225-235

Konya Bölgesinde Tularemi

Tularemia in Konya Region, Turkey

Şubat-Aralık 2010
2 epidemi (35 vaka) sporadik 5 vaka
Su orneklerinde kultur ve PCR ile *F.tularensis*
pozitifliği saptanmamış; ancak epidemi izlenen her iki bolgede de icme sularının klorlanmasında
aksaklıklar (şebeke suyuna, klorlama yapılmayan bir kaynak suyunun bağlanması gibi) olduğu izlenmiştir.

Özgün Çalışma/Original Article Mikrobiyol Bul 2014; 48(3): 413-419

Tularemi Türkiye'nin Kuzeyinden Güneyine Doğru Yayılıyor: Kahramanmaraş'da Küçük Bir Salgın

Tularemia is Spreading from North to South Side of Turkey: A Small Outbreak in Kahramanmaras, Turkey

21 Ekim 2013-22 Ocak 2014
10 hasta
Hastaların hiçbirinde kemirici hayvan veya dışkısıyla temas ve kene/ böcek sokma öyküsü saptanmamıştır
su örneklerinin hiçbirisinde polimeraz zincir reaksiyonu ile *F.tularensis* pozitifliği tespit edilmemiş; ancak su kaynaklarının hijyenik şartlarının yetersiz ve klorlama
işleminin uygunsuz olması nedeniyle salgının su kaynaklı olduğu düşünülmüştür

Original Article

Evaluation of tularemia cases focusing on the oculoglandular form

Sebnem Eren Gok[1], Aysel Kocagul Celikbas[1], Nurcan Baykam[1], Ayse Atay Buyukdemirci[1], Mustafa Necatı Eroglu[1], Ozlem Evren Kemer[2], Basak Dokuzoguz[1]

[1] *Infectious Diseases and Clinical Microbiology Department of Ankara Numune Training and Research Hospital, Ankara, Turkey*
[2] *Ophthalmology Department of Ankara Numune Training and Research Hospital, Ankara, Turkey*

Abstract

Introduction: Tularemia is a zoonotic disease caused by *Francisella tularensis*. The oculoglandular form is one of the rarest forms. In this

48 hasta

%81 orafaringeal
%14 okuloglanduler
%4 ülseroglanduler

Ateş, boğaz ağrısı ve LAP en sık semptomlar

Tüm hastalarda MAT (+)

Key words: tularemia; ocular involvement; tularemia outbreak.

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ORIGINAL ARTICLE INFECTIOUS DISEASES

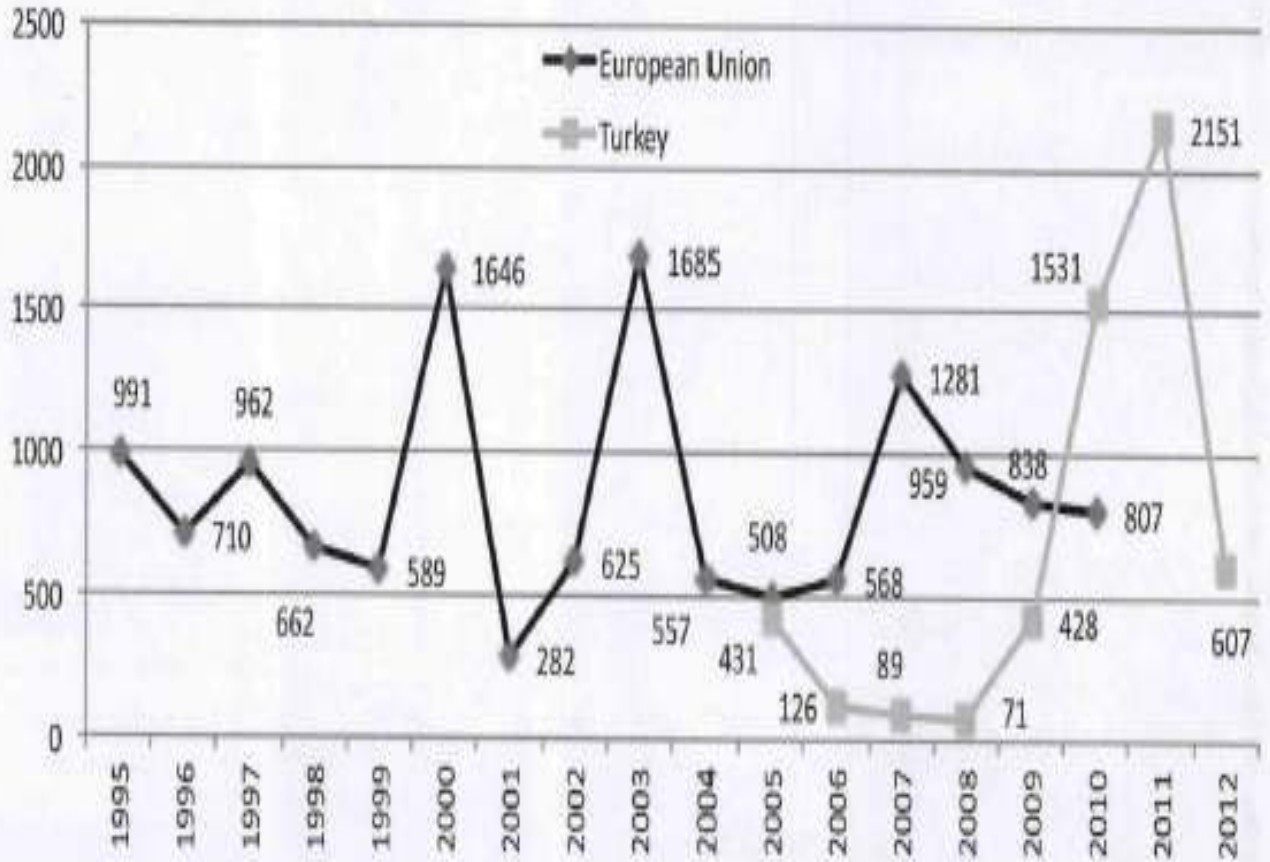
Evaluation of tularaemia courses: a multicentre study from Turkey

H. Erdem[1], D... umer[9], N. Tulek[10],
O. Ural[9], G. Y... k-Senturk[7], G.
Ertem-Tunce... C.
Ataman-Hati... Y. Kurtoglu-Gul[10],
N. Altin[7], S. C... rman[32], B. Teker[33],
H. Yilmaz[34], ... dem[26], A. Inan[2], Y.
Cag[29], S. Bol...
1) Department ... eases and Clinical
Microbiology, Ho... biology, Tekirdag State
Hospital, Tekirda... gy, School of Medicine,
Cumhuriyet Univ... ity, Zonguldak,
7) Department o... Infectious Diseases and
Clinical Microbio... Diseases and Clinical
Microbiology, Sd... raining and Research
Hospital, 11) Department of Infectious Diseases and Clinical Microbiology, School of Medicine, Ankara University, Ankara, 12) Department of Infectious Diseases

2000-2013
>17 yaş,
Serolojik olarak ya da kültürle doğrulamış vakalar
1034 vaka
%71' i kırsalda
En sık görülen klinik tablo orofaringeal tularemi
Servikal lenfadenomegali en sık görülen klinik tablo
Lenf nodlarının granülomatöz inflamasyonu en yaygın histopatolojik bulgu
Orofaringeal tulareminin en yaygın komplikasyonu lenf nodu süpürasyonu
Bu nedenle, tüberkülozun ayırıcı tanısı tularemi hastaları için önemli
En sık kullanılan antibiyotikler streptomisin ve doksisiklin.

TABLE 1. Monthly distribution of the tularemia cases in Turkey according to published literature

Regions	Years	Total number of the cases	Months												References
			December	January	February	March	April	May	June	July	August	September	October	November	
Kırklareli-Tekirdağ	1936	133							3	47	77	6			29
Bingöl-Tatvan-Reşadiye	1937	6									6				30
Kırklareli-Lüleburgaz	1945	15							2	5	7	1			31
Antalya-Bademağacı	1953	200									100	100			32
Bursa	1988-1998	205	Winter									Autumn			23
Ankara-Ayaş-Yağmurdede	1997	16	16												33
Düzce-Akçakoca	2000 and 2005	33			11		22								34
Bolu-Gerede-Yazıkara	2001	21										21			25
Amasya-Suluova	2004	86											86		35
Zonguldak-Kastamonu-Bartın		2004-2005	61		61										36
Kars-Sarıkamış	2004-2005	56			49							7			37
Kocaeli-Gölcük	2004-2005	145		145											38
Kocaeli-Karamürsel-Pazarköy	2005	17			17										39
Edirne-Lalapaşa-Demirköy	2005	10			10										24
Samsun-Havza	2005-2007	75	14	25	14	6	1				1		2	12	40
Sakarya-Kocadöngel	2005-2006	63			63										41
Bolu-Gerede-Nuhören	2006	6		6											42
Tokat	2005 and 2010	23	8					15							43, 44
Sivas	2008-2010	29	6	12	6	2								3	45
Çanakkale	2009	36	36												46
Çankırı-Çerkeş-Kadıözü	2009	18	16											2	47
Tekirdağ-Hayrabolu-Muzruplu	2010	8										8			28
Konya	2009-2010	40	21											19	48
Central Anatolia	2009-2011	139	23	23	38	29	10	1	3	3	7		2		49
Total number*	1936-2011	1441	210	176	249	115	32	22	13	55	198	177	124	70	
			(14.6)	(12.2)	(17.3)	(8)	(2.2)	(1.5)	(0.9)	(3.8)	(13.7)	(12.3)	(8.6)	(4.9)	


European Union
Turkey
2500
2000
1500
1000
500
0
991
962
710
662
589
1646
282
625
1685
557
508
431
568
126
1281
959
89
838
807
1531
71
428
2151
607
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012

Klinik

- İnkübasyon
  - 3-5 gün (max 2 hafta)
- Erken dönemde
  - Ateş
  - Döküntü
  - Miyalji
  - Artralji
  - Baş ağrısı

Klinik Formlar

- Ülseroglandüler
- Glandüler
- Okülоglandüler
- Pnömonik
- Tifoid
- Orofarengeal

Klinik Formlar

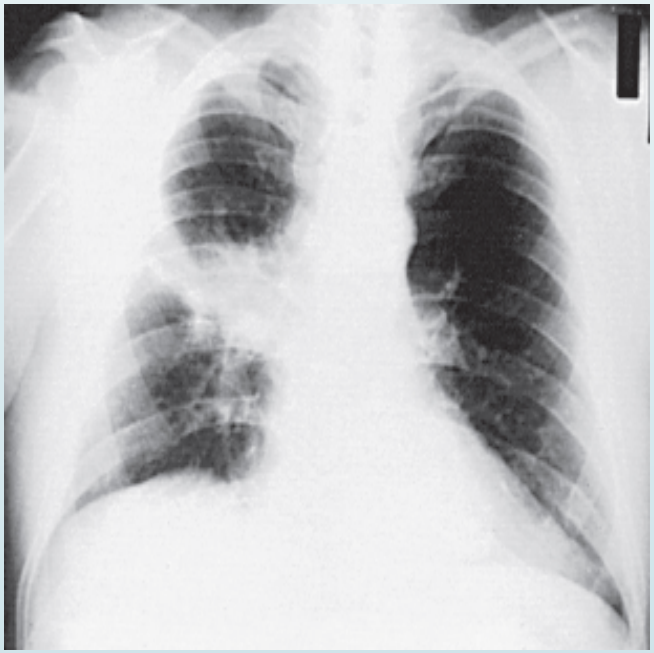
- **Ülsereglandüler tularemi**
  - Kronik ülserle birlikte
  - Genellikle cilt lezyonuyla uyumlu lenfadenopati ve süpürasyon
- **Glandüler tularemi**
  - Ülserin eşlik etmediği lenfadenopati

Klinik Formlar

- **Okülоglandüler tularemi**
- Okuler kontaminasyon sonrasında ağrılı konjonktivit
  - Ağrı, kaşınma, fotofobi, lakrimasyon,
  - Gözde konjesyon,
  - Konjonktival ödem ve
  - Mukopürülan akıntı
- Lokalize lenadenopati
  - Preauriküler
  - Submandibüler veya
  - Servikal

Klinik Formlar

- **Pnömonik tularemi**
- Bakterinin kan yoluyla ya da kontamine aerosollerin inhalasyonuyla akciğerle ulaşması
- Klinik belirtiler
  - Ateş, öksürük, substernal yanma yan ağrısı, balgam
- Hiler lenfadenopati
- Akciğer grafisi
  - Yama tarzında infiltrasyon
    - Bilateral olabilirler
  - Lober konsolidasyon
  - Plevral effüzyon



Klinik Formlar

- **Tifoidal tularemi**
- Semptomlar tifoyu taklit eder
- Ani başlangıçlı yüksek ateş
- Asteni
- Baş ağrısı
- Miyalji
- Nörolojik semptomlar
  - Konfüzyon
  - Stupor
  - Davranış değişiklikleri
- Lokalize lezyon yok

Klinik Formlar

- Orofarengeal tularemi
- Kontamine su ya da besin alımı sonucu kronik farenjit
- Mukozal ülserler
- Ağrılı, büyümüş servikal lenfadenopati

Komplikasyonlar

- Döküntüler
- Yumuşak doku abseleri
- Lenf nodu süpürasyonu
- Otitis media
- Osteomiyelit
- Hepatit
- Menenjit
- Beyin absesi

- İkincil döküntüler, tulareminin az tanınmış bir parçasıdır ve vakaların% 52'sinde bulunabilir.
- Genellikle semptomların ilk iki haftasında görülürler.

- Döküntü, kadınlarda erkeklerden daha yaygındır.
- Kutanöz değişiklikler
  - dağınık makülopapüler ve vesikülopapüler erüpsiyonlar,
  - püstüller,
  - eritema nodozum,
  - eritema multiforme,
  - akneiform lezyonlar ve ürtiker olabilir.

INFECTIOUS DISEASES, 2016
http://dx.doi.org/10.1080/23744235.2016.1222546

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CASE REPORT

Francisella tularensis endocarditis: two case reports and a literature review

Rostane Gaci[a], Corentine Alauzet[b], Christine Selton-Suty[c], Alain Lozniewski[b], Céline Pulcini[a,d], Thierry May[a] and François Goehringer[a]

Vaka 1
Öksürük ve ateş yakınmaları
Cilt lezyonu LAP yok
BT de septik emboli
TEE Triküspit kapakta vetetasyon
Kan kültüründe *F. tularensis* holarctica biovar 1
Vaka 2
Ateş, kilo kaybı, halsizlik
Cilt lezyonu LAP yok
Romatizmal kalp hastalığı mitral kapak değişimi
Kalp pili, DM, alkol
TEE atrial kapakta vejetasyon
Kan kültüründe *F. tularensis* holarctica

BMJ Case Rep. 2017 Oct 11;2017. pii: bcr-2017-221258. doi: 10.1136/bcr-2017-221258.

Unusual case of prosthetic joint infection caused by Francisella Tularensis.

Rawal H[1], Patel A[2], Moran M[3].

⊕ Author information

Abstract

Tularaemia is a zoonotic infection caused by *Francisella tularensis*.Ulceroglandular, glandular, oculoglandular, pharyngeal, typhoidal and pneumonic types are the different types of the disease. Infection of prosthetic joints occurs at an exceedingly uncommon rate. We report a case of prosthetic joint infection involving the hip with *F. tularensis*, which to the best of our knowledge after a thorough literature review is the second of its kind.

KEYWORDS: bone and joint infections; infections

PMID: 29025776 DOI: 10.1136/bcr-2017-221258

Laboratuvar

- Lökosit normal/lökositoz
- Sedimantasyon yükselebilir
- CRP yükselebilir
- AST, ALT yükselebilir
- Trombositopeni,
- Na düşüklüğü,
- Pyüri,
- Renal yetmezlik,miyoglobinüri bildirilmiştir.

Tanı

- Kültür
  - Altın standart
  - Güvenlik kabini
  - Sistin/sistein içeren besi yerleri
- ELISA ve aglütinasyon testleri
- Direkt Florasan Antikor (DFA)
- İmmunohistokimyasal boyamalar
- PCR

Tanı

Örnek	Çalışma Yöntemi
Boğaz sürüntüsü	Kültür, DFA
Lenf nodu aspirasyonu	Kültür, DFA
Deri lezyonu, yara sürüntü örneği	Kültür, DFA
Doku biyopsi örneği	Kültür, DFA
Balgam	Kültür, DFA
Mide yıkama sıvısı	Kültür, DFA
Kan/kemik iliği	Kültür, DFA
Otopsi materyali	Kültür, DFA
İzolat	*F. tularensis* tür/alt tür tayini Konvansiyonel yöntem, PCR
İzolat	Antibiyotik duyarlılık testi E-test, dilüsyon yöntemleri
Serum	Serolojik tanı Mikro-aglütinasyon/tüp aglütinasyon ELISA IgM-G Western-Blot

Ayırıcı Tanı-Garanülomatöz Lenfadenit

- Non-infeksiyöz
  - Sarkoidoz lenadenit
  - Sarkoidoz benzeri lenfadenit
  - Beryliosiz
- İnfeksiyöz
  - Süpüratif
    - Tularemi
    - Kedi tırmığı
    - Yersinia
    - Lenfogronuloma venorum
    - Fungal
  - Non-Süpüratif
    - Tuberkuloz
    - Atipik mikobakteri
    - BCG lenadeniti
    - Toxo
    - Lepra
    - Sifiliz
    - Bruselloz
    - Fugal

Assano S. Granolomatous Lymphadenitis. J Clin Exp Hemathopathol. Vol 52, No 1, 2012.

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Tuberculosis or tularemia? A molecular study in cervical lymphadenitis☆

Şükrü Yıldırım [a], Vedat Turhan [b,*], Aynur Karadenizli [c], Yalçın Önem [d], Ergenekon Karagöz [b], Cafer Eroğlu [e], Faruk Çiftçi [f]

[a] Pathology Laboratory, Bursa Military Hospital, Bursa, Turkey
[b] Department of Infectious Diseases and Clinical Microbiology, GATA Haydarpaşa Training Hospital, Istanbul, Turkey
[c] Department of Medical Microbiology, Kocaeli University, Kocaeli, Turkey
[d] Department of Internal Medicine, GATA Haydarpaşa Training Hospital, Istanbul, Turkey
[e] Department of Infectious Diseases and Clinical Microbiology, Samsun 19 Mayıs University, Samsun, Turkey
[f] Department of Tuberculosis and Chest Diseases, GATA Haydarpaşa Training Hospital, Istanbul, Turkey

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Francisella tularensis
Cervical lymphadenitis

SUMMARY

Background: Over the last two to three decades there has been a marked decrease in certain bacterial infections in Turkey. One of them is tuberculosis. Of note, statistics published by the Turkish Ministry of Health (MoH) show decreasing pulmonary tuberculosis (PTB), but on the other hand, increasing extrapulmonary tuberculosis (EPTB). The most common form of EPTB is tuberculous cervical lymphadenitis (TCL). The increase in the number of TCL cases despite the decline in cases of PTB is seen as a paradoxical issue. In contrast there has been an increase in the number of oropharyngeal tularemia cases in the last decade in Turkey. The aim of this study was to draw attention to the importance of differentiating between TCL and tularemia lymphadenitis, because these diseases may have a similar histopathological appearance.

Methods: Thirty-two cases diagnosed as TCL were identified from the archives of a pathology laboratory (Patomer Pathology Laboratory, Bursa, Turkey). PCR tests for *Francisella tularensis* and *Mycobacterium tuberculosis* were carried out on the paraffin tissue blocks of these cases. At the same time, statistical data

1996-2010
Pulmoner ve ekstra pulmoner Tuberkuloz lenadenit tanılı 32 vaka
Kezeifiye granülomatöz lenafedenit patolojik tanı
6 vakada (%19) Tularemi için PCR (+)

Cervical lymphadenitis: tuberculosis or tularaemia?†

O. Karabay[1], S. Kilic[2], S. Gurcan[3], T. Pelitli[4], A. Karadenizli[5], H. Bozkurt[6] and S. Bostanci[5]

1) Department of Infectious Diseases, Sakarya University Medical Faculty, Sakarya, 2) Refik Saydam National Public Agency, National Tularemia Reference Laboratory, Ankara, 3) Department of Medical Microbiology, Trakya University Medical Faculty, Edirne, 4) Primary Health General Directorate, Department of Zoonotic Diseases, Turkish Ministry of Health, Ankara, 5) Department of Medical Microbiology, Kocaeli University Medical Faculty, Kocaeli and 6) Tuberculosis Control Department, Turkish Ministry of Health, Ankara, Turkey

Parameters	TCL diagnosed group N (%)	Controls N (%)	p
N (1766)	1170	596	
Tularaemia positivity (any titre)	96 (8.2%)	4 (0.7%)	< 0.001
Tularaemia positivity (>1/80)	79 (6.7%)	2 (0.3%)	< 0.001

TCL, cervical tuberculosis lymphadenopathy.

Abstract

Both tuberculosis cerv ms and pathological findings. We aimed to investiga m the Tuberculosis Control Dispensaries between ut and included in the study. Control group subject d consent was obtained, the sera obtained from volunteer TCL patients and the control group were tested with a microagglutination technique for *Francisella tularensis*. Antibodies to *Brucella* were also investigated with a tube agglutination test for cross-reactivity in sera that were seropositive for tularaemia. Sera were obtained from a total of 1170 individuals in the TCL group and 596 in the control group from 67 of 81 provinces in Turkey. *Francisella tularensis*-positive antibodies were found in 79 (6.75%) cases in the TCL group and two (0.33%) cases in the control group with a

2008-2011
229 verem savaş dispanserinde extra torasik tuberkuloz lenadenit tanılı 1170 gönüllüden kan örneği alınmış
Sağlıklı kan donörleri kontrol grubu (n:596)
Tularemi referans laboratuvarında MAT ile taranmış.

Clin Microbiol Infect 2013; **19:** E113–E117
10.1111/1469-0691.12097

Tedavi

Endikasyon ve Hasta Grubu	Önerilen Antibiyotikler ve Dozları
Orta-Ağır Hastalık	
Erişkin	Streptomisin 10 mg/kg IM q12 sa 7-10 gün Gentamisin 5 mg/kg/gün IM veya IV 8 saate 7-10 gün
Çocuk	Streptomisin 15-20 mg/kg IM q12 sa 7-10 gün Gentamisin 5 mg/kg/gün IM veya IV 8-12 saate 7-10 gün
Hafif Hastalık	
Erişkin	Siprofloksasin 2x500 mg PO 14 gün Doksisiklin 2x100 mg PO 14 gün
Çocuk	Gentamisin 5 mg/kg/gün IM veya IV 8-12 saate 7-10 gün Doksisiklin 2-4 mg/kg/gün 14 gün

Tedavi

- Gebelerde
  - Gentamisin
    - 5 mg/kg İM/İV/gün
  - Streptomisin
    - 2X1 g İM/gün
  - Doksisiklin
    - 2X100 mg İV/gün
  - Siprofloksasin
    - 2X400 mg İV/gün

Yilmaz GR, Guven T, Gruner R, et al. Tularemia during pregnancy: three cases. *Vector Borne Zoonotic Dis*. 2014;14:171-173.
Yeşilyurt M, Kiliç S, Çelebi B, et al. Tularemia during pregnancy: report of four cases. *Scand J Infect Dis*. 2013;45:324-328.
Dentan C, Pavese P, Pelloux I, et al. Treatment of tularemia in pregnant woman, France. *Emerg Infect Dis*. 2013;19:996-998.

Profilaksi

Erişkinlerde	Doksisiklin 2x100 mg PO 14 gün Siprofiloksasin 2x500 mg PO 14 gün
Çocuklarda	Doksisiklin <45 kg 2,2 mg/kg/gün >45 kg 2x100 mg PO Siprofiloksasin 15mg/kg/gün

Aşı

- WHO' nun yaptığı öngürüye göre 50 kg *F. tularensis* ile
  - 5 milyon nüfuslu bir bölgede
  - En az 250000 sakat kişi
  - 19000 ölüm

WHO Consultant Group. Health aspects of chemical and biological weapons. 1970; 105-7.

Virulence 4:8, 859–870; November 15, 2013; © 2013 Landes Bioscience

Immunotherapy for tularemia

Table 2A. Immune agonists that confer protection against virulent *Francisella* infection

Agonist	Cellular receptor	Challenge strain, route, animal	Protective effect	Requirements for protection
Acai PS	TLR4? Carbohydrate Receptors?	Mice infected via aerosol with SchuS4	i.n. pre- or post-treatment increased survival rates	IFN-γ
CLDC+MPF	TLR9+DAI	Mice infected i.n. with SchuS4	i.v. pre-treatment increased survival rate	RNS/ROS
MPL	TLR4	Mice infected i.n. with LVS or SchuS4	i.p. pre-treatment increased survival rates in animals challenged with either strain.	ND
Yeast glucans	Carbohydrate receptors?	Rats infected i.p. with SchuS4	i.v. pre-treatment increased survival rate	ND
Poly I:C	TLR3	Mice infected i.n. with LVS or SchuS4	i.n. pre- or post-treatment extended mean time to death in LVS- and SchuS4-challenged animals	ND
CLDC	TLR9+DAI	Mice infected i.n. with LVS or SchuS4	i.n. pre-treatment increased survival rates in LVS-challenged mice and extended mean time to death in SchuS4-challenged mice	IFN-γ, NK cells (LVS-challenged mice)

See text for references. ?, cellular receptor unknown or unclear; ND, not determined; [a]strain used for challenge unclear.

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Live Attenuated Tularemia Vaccines: Recent Developments and Future Goals

Intracellular growth characteristics of live attenuated Schu S4 mutants.

Gene	Function	Intracellular Phenotype	Cell Types Tested	Reference
FTT_0918	58 kDa protein	Fails to replicate to wild type levels in murine macrophages	murine PEC	[63]
FTT_0107c/*dsbB*	Disulfide bond formation	Fails to replicate	J774A.1, HepG2	[71]
fipB	Lipoprotein	Fails to replicate in hepatic cells, does not escape phagosome in macrophages	HepG2, J774A.1	[36]
purMCD	Purine biosynthesis	Fails to replicate	human MDM, A549	[17]
guaA, *guaB*	GMP synthesis	Fails to replicate	J774A.1	[72]
katG	Catalase	Similar growth to wild type	murine PEC	[18]
capB	Capsule biosynthesis	Similar growth to wild type	J774A.1	[21]
clpB	Heat shock protein	Not determined	N/A	[31]
ggt	Gamma-glutamyl transpeptidase	Fails to replicate	J774A.1	[34]
FTT_0615c	Spermine responsiveness	Similar growth to wild type	murine BMDM, human MDM	[28]
FTT_0369c, FTT_1676	Unknown	Fail to replicate	murine BMDM	[35]

Aşı

- LVS aşısı
  - *F. tularensis holarctica*
  - Hücresel ve humoral bağışıklık
  - Tifoidal hastalığa karşı koruyucu ancak ülseroglandüler forma karşı koyuculuğu yok
  - *F. tularensis tularensis* ile gelişen pnömonik forma etkisiz
  - Aerosol veya intranazal yolla verildiğinde etkinliği artıyor
- Schu 4
  - *F. tularensis tularensis*

Özetle…

- Ülkemizde ayırıcı tanıda mutlaka akılda tutulması gereken bir ajan
- Tedavi edilebilir
- Komplikasyonlar
- Biyolojik silah potansiyeli

Teşekkürler...